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Sirolimus-associated regression of benign lymphangioendothelioma

To the Editor: Benign lymphangioendothelioma (BL, acquired progressive lymphangioma) is a rare, slowly growing lymphatic neoplasm with wide age distribution appearing most commonly in middle-aged and older adults. BL typically presents as an asymptomatic, well-circumscribed plaque with red to bruise-like coloration on which small papules may arise. BL most often occurs on the thigh (33%), but has also appeared on the head and neck (20.5%), upper limb (20.5%), trunk (18%), and shoulder (8%).[1]

Histologically, BL demonstrates anastomosing, cleft-like, thin-walled vascular channels dissecting through collagen bundles.[1,2] The vascular spaces may isolate preexisting vascular or adnexal structures resembling the promontory sign seen in patch stage Kaposi sarcoma. The vessels are lined by a monolayer of endothelial cells with no cytologic atypia or increased mitoses. Papillary projections resembling endothelial hyperplasia are sometimes noted. D2-40—positive immunofluorescence indicates the lymphatic cell origin of BL.[2] Recent findings have shown that vascular endothelial growth factor (VEGF), a well-known angiogenic growth factor, promotes lymphogenesis by upregulating mammalian target of rapamycin (mTOR)/p70S6K signaling and therefore may play a role in the development of BL.[3] BL treatment has typically been limited to surgical excision for small lesions, although disease recurrence is common.[1]

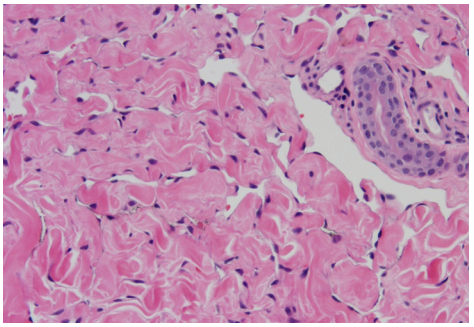

Fig 1. Benign lymphangioendothelioma. Vascular spaces within the deep dermis demonstrate a slit-like appearance. (Hematoxylin-eosin stain; original magnification: ×200.)

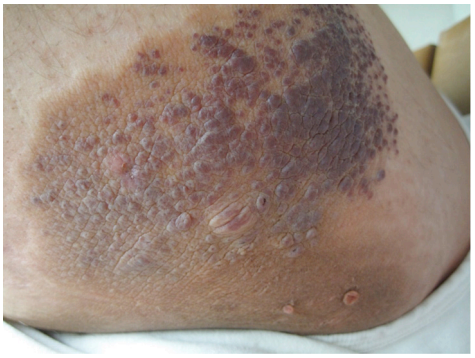

Fig 2. Benign lymphangioendothelioma. Light brown papules coalescing into a 5- × 6-cm plaque on the patient's medial left thigh.

A 48-year-old man who had undergone allograft kidney transplantation at age 38 presented for evaluation of a large, slowly growing plaque on his left thigh which was present since childhood. Since transplantation, he had been on an immunosuppression regimen of tacrolimus, mycophenolate mofetil, and prednisone. During this period, the plaque enlarged substantially, prompting his initial visit to a dermatologist. On examination, dusky brown to bluish-red dermal papules coalesced into a 10- × 10-cm plaque overlying his medial left thigh.

Punch biopsy showed a proliferation of thin, irregular vascular spaces involving the entire dermis. These spaces had a lobular arrangement superficially and a more slit-like appearance deeper in the dermis (Fig 1). No endothelial cell atypia was present and HHV-8 polymerase chain reaction was negative. The biopsy was reviewed by 4 board-certified dermatopathologists, including a vascular expert in consultation, and the diagnosis of BL was confirmed.

Before the patient's diagnostic biopsy, his transplant team suspected Kaposi sarcoma, given the clinical appearance of the plaque. Given the team's clinical experience demonstrating slowed Kaposi sarcoma disease progression in some cases, sirolimus was empirically substituted for tacrolimus. Even though the patient's diagnosis was ultimately confirmed as BL, sirolimus was continued because the thigh plaque improved clinically. After 7.5 months, the patient's lesion had decreased in size, stabilized at 5 × 6 cm, lightened in color, and flattened significantly (Fig 2).

Other reports have demonstrated the efficacy of this drug in the treatment of lymphovascular proliferative disorders such as Kaposiform hemangioendothelioma and diffuse lymphangiomatosis.[4,5] Evidence suggests that VEGF plays a role in lymphogenesis by upregulating mTOR signaling. Recent studies have shown that sirolimus inhibits lymphogenesis by decreasing synthesis and promoting degradation of VEGF receptor 3 (VEGFR-3).[3] Taken together, these findings suggest that, by targeting VEGFR-3, sirolimus may represent an important therapeutic option for patients with symptomatic BL and, importantly, other lymphovascular proliferations with malignant or life-threatening potential.

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The role of infliximab in the treatment of superficial granulomatous pyoderma of the head and neck

To the Editor: Superficial granulomatous pyoderma (SGP) is a rare, chronic inflammatory disorder.[1] Although considered a superficial, vegetative variant of pyoderma gangrenosum (PG), SGP exhibits important differences (Fig 1, *A*).[1,2] Moreover, SGP responds favorably to therapy, except in cases of SGP involving the head and neck.[1] We present a patient with SGP on the face, neck, and trunk treated with combined infliximab and topical tacrolimus, and review all systemic therapies reported, to our knowledge, in the treatment of SGP of the head and neck.

An 83-year-old Caucasian man with extensive history of cardiovascular disease presented for nonhealing ulcers of more than 1 year's duration on the right temple, right postauricular neck, and central chest (Fig 1, *B*). Each lesion evolved after a surgical procedure as slowly growing ulcerative plaques for which multiple therapies were attempted but unsuccessful, including surgical debridement, skin grafting, and hyperbaric oxygen. The patient was on oral prednisone 20 mg daily upon presentation in early November 2010 and had failed several oral antibiotics. Prior biopsies of the right temple and chest were read by an outside